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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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10/533,670

12/30/2005

Eswaran Krishnan Iyer

WH-3

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07/18/2008

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LORTON, VA 22079

EXAMINER

PURDY, KYLE A

ART UNIT

PAPER NUMBER

1611

MAIL DATE

DELIVERY MODE

07/18/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|------------------------------------|--|
| Office Action Summary | Application No. 10/533,670 | Applicant(s) IYER ET AL. | |
| | Examiner Kyle Purdy | Art Unit 1611 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05/03/2005, 01/11/2008 and 05/07/2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14-81 is/are pending in the application.
- 4a) Of the above claim(s) 14-72 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 73-81 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application

1. The Examiner acknowledges receipt of the amendments filed on 05/07/2008 wherein claims 1-13 have been cancelled and claims 73-81 have been newly added.
2. Claims 14-81 are pending and are claims 73-81 are presented for examination on the merits. The following rejections are made.

Response to Applicants' Arguments

3. Applicants arguments and amendments filed 05/07/2008 regarding the rejection of claims 7 and 8 made by the Examiner under 35 USC 112, 2nd paragraph have been fully considered and due to the cancellation of previously examined claims, are found persuasive. This rejection is hereby withdrawn.
4. Applicants arguments and amendments filed 05/07/2008 regarding the rejection of claims 1-13 made by the Examiner under 35 USC 103(a) over Whitcomb (US 6011049) in view of Pearson et al. (US 2003/0078269) have been fully considered and due to the cancellation of all previously examined claims are found persuasive. This rejection is hereby withdrawn.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 73-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitcomb et al. (US 6011049; of record) in view of Timmins et al. (WO 99/47128), Timmins et al. (US 6031004) and Antarker et al. (US 20060057202).

7. Whitcomb discloses a pharmaceutical combination for treating diabetes wherein the combination includes a glitazone, a biguanide and a sulfonylurea (see instant claim 73). It is taught that the therapeutic composition comprising these ingredients are especially useful for treating diabetes and associated complications such as cardiovascular disease and retinopathy. The mode by which the compounds are administered includes a single triple-combination dosage or administered individually (i.e. physically separated) as performed clinically, and exemplified dosage forms include tablets, capsules as wells controlled release formulations (see column 4, lines 35-40; see instant claim 73).

8. Whitcomb fails to teach however the biguanide as being a slow release component, the sulfonylurea as being either slow or immediate release and the glitazone as being immediate release.

9. Timmins (herein '128) is directed to a biphasic controlled release delivery system for high solubility pharmaceuticals such as the biguanide metformin. The composition comprises hydrophilic polymers (hydroxypropyl methylcellulose), hydrophobic polymers (ethylcellulose and microcrystalline cellulose) and hydrophobic materials (waxes and fatty alcohols) (see abstract and pages 17-18; see instant claims 73-76). Example 4 teaches a composition which comprises about 50% metformin (see instant claim 78) as well as possess a hydrophilic:hydrophobic polymer component at a ratio of 9:1 (see instant claim 77).

10. The teaching of Timmins (herein '004) is directed to salts of metformin (a biguanide). It is disclosed that salts of metformin are less soluble in water and provide an opportunity for formulating controlled release systems to achieve a desired release rate (see column 2, line 40). Example 8 for instance teaches a sustained release composition which comprises metformin and glipizide (a sulfonylurea) (see instant claim 73). It also comprises microcrystalline cellulose (hydrophobic polymer) and hydroxypropyl methylcellulose (hydrophilic polymer) at a weight ratio of about 1:2 (see instant claims 73, 74 and 77). The metformin is present at about 85% by weight of the composition (see instant claim 78) and the glipizide is present at about 0.7% by weight (see instant claim 79).

11. Antarkar is directed to multilayer tablets containing thiazolidinediones (i.e. glitazone) and optionally biguanides for immediate release (see abstract; see instant claim 73). In the compositions the glitazone can comprise from 5-50% of the compositions weight (see instant claim 80). Additionally, in Example 1 it is disclosed that microcrystalline cellulose and hydroxypropylmethylcellulose are used at a weight ratio of about 20:1 and Example 3 teaches a sustained release composition for metformin wherein methacrylic acid (hydrophobic) and hydroxypropylmethylcellulose are used at a weight ratio of about 1:2.5 (see instant claim 77).

12. It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Whitcomb with 128, 004, Antarkar with a reasonable expectation for success in arriving at an oral delivery system comprising a slow release biguanide component, a slow or rapid release sulfonylurea component and an immediate release glitazone component. The teaching of Whitcomb specifically discloses the use of these three class of compounds as useful together and stipulates for them to be formulated into sustained and

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rapid release composition. Whitcomb however does not set forth which components are to be sustained and immediately released not does it set forth any specific details regarding the component amounts or the presence of additional hydrophobic/hydrophilic excipients. 128 discloses a slow release biguanide composition useful for the gastrointestinal release. It teaches that the composition can comprises a hydrophilic polymer, a hydrophobic polymer and a hydrophobic material. The teaching of 004 is directed to novel slow release compositions for metformin and sulfonylureas. Timmins sets forth specific weight percentages for these two ingredients (see above) which obviate the instantly claimed amounts. Moreover, it also sets forth excipient requirements (see above) which obviate the instant claim requirements. Antarkar teaches compositions for the immediate release of glitazones. Its disclosure also obviates the instant claims limitations with respect to weight percentage (see above) in the composition. As all of the features of the instant application are disclosed in the prior art and because there is a clear motivation to combine their features, one of ordinary skill in the art would have a reasonable expectation for success in combining the references above to arrive at the instantly claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

14. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

16. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

17. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*/Kyle Purdy/
Examiner, Art Unit 1611
July 9, 2008*

*/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615*